

University of Dundee

## THE CONCISE GUIDE TO PHARMACOLOGY 2021/22

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A diagram of a cell membrane cross-section. The membrane is represented by a phospholipid bilayer. Various proteins are embedded or attached to the surface. On the left, a yellow hexagon with a 'V' is attached to a pink protein. In the center, a blue double-headed arrow indicates movement across the membrane. To the right, a blue Y-shaped protein is shown. Below it, a purple protein is embedded. Further right, a pink protein with blue dots is shown. At the bottom, a green coiled protein is on the left, and a blue coiled protein is on the right. A central purple sphere with a blue 'N' and a yellow helix is also present.

**Abstract**

The Concise Guide to PHARMACOLOGY 2021/22 is the fifth in this series of biennial publications. The Concise Guide provides concise overviews, mostly in tabular format, of the key properties of nearly 1900 human drug targets with an emphasis on selective pharmacology (where available), plus links to the open access knowledgebase source of drug targets and their ligands ([www.guidetopharmacology.org](http://www.guidetopharmacology.org)), which provides more detailed views of target and ligand properties. Although the Concise Guide constitutes over 500 pages, the material presented is substantially reduced compared to information and links presented on the website. It provides a permanent, citable, point-in-time record that will survive database updates. The full contents of this section can be found at <http://onlinelibrary.wiley.com/doi/bph.15537>. In addition to this overview, in which are identified 'Other protein targets' which fall outside of the subsequent categorisation, there are six areas of focus: G protein-coupled receptors, ion channels, nuclear hormone receptors, catalytic receptors, enzymes and transporters. These are presented with nomenclature guidance and summary information on the best available pharmacological tools, alongside key references and suggestions for further reading. The landscape format of the Concise Guide is designed to facilitate comparison of related targets from material contemporary to mid-2021, and supersedes data presented in the 2019/20, 2017/18, 2015/16 and 2013/14 Concise Guides and previous Guides to Receptors and Channels. It is produced in close conjunction with the Nomenclature and Standards Committee of the International Union of Basic and Clinical Pharmacology (NC-IUPHAR), therefore, providing official IUPHAR classification and nomenclature for human drug targets, where appropriate.

**Conflict of interest**

The authors state that there are no conflicts of interest to disclose.

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**Table of contents****S1 Introduction and Other Protein Targets**

S8 Adiponectin receptors  
S9 Aryl hydrocarbon receptor  
S10 Non-enzymatic BRD containing proteins  
S11 CD molecules  
S13 Methyllysine reader proteins  
S14 Fatty acid-binding proteins  
S16 Notch receptors  
S17 Regulators of G protein Signaling (RGS) proteins  
S17 RZ family  
S18 R4 family  
S19 R7 family  
S19 R12 family  
S20 Sigma receptors  
S21 Transthyretin  
S22 Tubulins  
S23 SARS-CoV-2  
S23 Structural proteins  
S24 Polyproteins  
S24 Proteases  
S25 Nucleic acid turnover  
S25 Other proteins

**S27 G protein-coupled receptors**

S31 Orphan and other 7TM receptors  
S32 Class A Orphans  
S41 Class C Orphans

S41 Opsin receptors  
S42 Taste 1 receptors  
S43 Taste 2 receptors  
S44 Other 7TM proteins  
S45 5-Hydroxytryptamine receptors  
S48 Acetylcholine receptors (muscarinic)  
S50 Adenosine receptors  
S52 Adhesion Class GPCRs  
S55 Adrenoceptors  
S59 Angiotensin receptors  
S60 Apelin receptor  
S61 Bile acid receptor  
S62 Bombesin receptors  
S63 Bradykinin receptors  
S64 Calcitonin receptors  
S66 Calcium-sensing receptor  
S67 Cannabinoid receptors  
S68 Chemerin receptors  
S69 Chemokine receptors  
S73 Cholecystokinin receptors  
S74 Class Frizzled GPCRs  
S76 Complement peptide receptors  
S78 Corticotropin-releasing factor receptors  
S79 Dopamine receptors  
S81 Endothelin receptors  
S82 G protein-coupled estrogen receptor  
S83 Formylpeptide receptors

S84 Free fatty acid receptors  
S86 GABAB receptors  
S87 Galanin receptors  
S89 Ghrelin receptor  
S90 Glucagon receptor family  
S91 Glycoprotein hormone receptors  
S92 Gonadotrophin-releasing hormone receptors  
S93 GPR18, GPR55 and GPR119  
S94 Histamine receptors  
S96 Hydroxycarboxylic acid receptors  
S97 Kisspeptin receptor  
S98 Leukotriene receptors  
S100 Lysophospholipid (LPA) receptors  
S101 Lysophospholipid (S1P) receptors  
S103 Melanin-concentrating hormone receptors  
S104 Melanocortin receptors  
S105 Melatonin receptors  
S106 Metabotropic glutamate receptors  
S108 Motilin receptor  
S110 Neuromedin U receptors  
S111 Neuropeptide FF/neuropeptide AF receptors  
S112 Neuropeptide S receptor  
S113 Neuropeptide W/neuropeptide B receptors  
S114 Neuropeptide Y receptors  
S116 Neurotensin receptors  
S117 Opioid receptors  
S119 Orexin receptors

S120	Oxoglutarate receptor	S233	Volume regulated chloride channels	S289	Type I RTKs: ErbB (epidermal growth factor) receptor family
S120	P2Y receptors	S234	Connexins and Pannexins	S290	Type II RTKs: Insulin receptor family
S123	Parathyroid hormone receptors	S236	Piezo channels	S291	Type III RTKs: PDGFR, CSFR, Kit, FLT3 receptor family
S124	Platelet-activating factor receptor	S237	Sodium leak channel, non-selective	S292	Type IV RTKs: VEGF (vascular endothelial growth factor) receptor family
S125	Prokineticin receptors	S238	Orai channels	S293	Type V RTKs: FGF (fibroblast growth factor) receptor family
S126	Prolactin-releasing peptide receptor	<b>S245 Nuclear hormone receptors</b>		S294	Type VI RTKs: PTK7/CCK4
S127	Prostanoid receptors	S247	1A. Thyroid hormone receptors	S294	Type VII RTKs: Neurotrophin receptor/Trk family
S129	Proteinase-activated receptors	S248	1B. Retinoic acid receptors	S295	Type VIII RTKs: ROR family
S131	QRFP receptor	S249	1C. Peroxisome proliferator-activated receptors	S296	Type IX RTKs: MuSK
S132	Relaxin family peptide receptors	S250	1D. Rev-Erb receptors	S296	Type X RTKs: HGF (hepatocyte growth factor) receptor family
S134	Somatostatin receptors	S251	1F. Retinoic acid-related orphans	S297	Type XI RTKs: TAM (TYRO3-, AXL- and MER-TK) receptor family
S135	Succinate receptor	S252	1H. Liver X receptor-like receptors	S297	Type XII RTKs: TIE family of angiopoietin receptors
S136	Tachykinin receptors	S253	1I. Vitamin D receptor-like receptors	S298	Type XIII RTKs: Ephrin receptor family
S137	Thyrotropin-releasing hormone receptors	S254	2A. Hepatocyte nuclear factor-4 receptors	S299	Type XIV RTKs: RET
S138	Trace amine receptor	S255	2B. Retinoid X receptors	S299	Type XV RTKs: RYK
S139	Urotensin receptor	S255	2C. Testicular receptors	S300	Type XVI RTKs: DDR (collagen receptor) family
S140	Vasopressin and oxytocin receptors	S256	2E. Tailless-like receptors	S300	Type XVII RTKs: ROS receptors
S142	VIP and PACAP receptors	S256	2F. COUP-TF-like receptors	S301	Type XVIII RTKs: LMR family
<b>S157 Ion channels</b>		S257	3B. Estrogen-related receptors	S301	Type XIX RTKs: Leukocyte tyrosine kinase (LTK) receptor family
S159	Ligand-gated ion channels	S257	4A. Nerve growth factor IB-like receptors	S302	Type XX RTKs: STYK1
S160	5-HT <sub>3</sub> receptors	S258	5A. Fushi tarazu F1-like receptors	S302	Receptor serine/threonine kinase (RSTK) family
S162	Acid-sensing (proton-gated) ion channels (ASICs)	S259	6A. Germ cell nuclear factor receptors	S303	Type I receptor serine/threonine kinases
S165	Epithelial sodium channel (ENaC)	S259	0B. DAX-like receptors	S304	Type II receptor serine/threonine kinases
S166	GABA <sub>A</sub> receptors	S260	Steroid hormone receptors	S304	Type III receptor serine/threonine kinases
S172	Glycine receptors	S260	3A. Estrogen receptors	S305	RSTK functional heteromers
S175	Ionotropic glutamate receptors	S261	3C. 3-Ketosteroid receptors	S306	Receptor tyrosine phosphatase (RTP) family
S180	IP <sub>3</sub> receptors	<b>S264 Catalytic receptors</b>		S308	Tumour necrosis factor (TNF) receptor family
S181	Nicotinic acetylcholine receptors	S266	Cytokine receptor family	<b>S313 Enzymes</b>	
S185	P2X receptors	S266	IL-2 receptor family	S318	Acetylcholine turnover
S187	ZAC	S268	IL-3 receptor family	S318	Adenosine turnover
S188	Voltage-gated ion channels	S268	IL-6 receptor family	S321	Amino acid hydroxylases
S188	CatSper and Two-Pore channels	S270	IL-12 receptor family	S322	L-Arginine turnover
S190	Cyclic nucleotide-regulated channels	S271	Prolactin receptor family	S336	2.1.1.- Protein arginine N-methyltransferases
S192	Potassium channels	S272	Interferon receptor family	S322	Arginase
S193	Calcium- and sodium-activated potassium channels	S273	IL-10 receptor family	S323	Arginine:glycine amidinotransferase
S195	Inwardly rectifying potassium channels	S274	Immunoglobulin-like family of IL-1 receptors	S323	Dimethylarginine dimethylaminohydrolases
S199	Two-pore domain potassium channels	S275	IL-17 receptor family	S324	Nitric oxide synthases
S201	Voltage-gated potassium channels	S276	GDNF receptor family	S325	Carbonic anhydrases
S204	Ryanodine receptors	S277	Integrins	S325	Carboxylases and decarboxylases
S205	Transient Receptor Potential channels	S281	Pattern recognition receptors	S326	Carboxylases
S219	Voltage-gated calcium channels	S281	Toll-like receptor family	S327	Decarboxylases
S222	Voltage-gated proton channel	S283	NOD-like receptor family	S328	Catecholamine turnover
S223	Voltage-gated sodium channels	S285	RIG-I-like receptor family	S330	Ceramide turnover
S225	Aquaporins	S285	Receptor guanylyl cyclase (RGC) family		
S227	Chloride channels	S286	Transmembrane guanylyl cyclases		
S228	ClC family	S287	Nitric oxide (NO)-sensitive (soluble) guanylyl cyclase		
S230	CFTR	S288	Receptor tyrosine kinases (RTKs)		
S231	Calcium activated chloride channel				
S232	Maxi chloride channel				

S331	Serine palmitoyltransferase	S373	Inositol 1,4,5-trisphosphate 3-kinases	S405	2.5.1.58 Protein farnesyltransferase
S331	Ceramide synthase	S373	Inositol polyphosphate phosphatases	S405	3.5.3.15 Peptidyl arginine deiminases (PADI)
S332	Sphingolipid $\Delta 4$ -desaturase	S374	Inositol monophosphatase	S406	3.6.5.2 Small monomeric GTPases
S332	Sphingomyelin synthase	S374	Kinases (EC 2.7.x.x)	S406	RAS subfamily
S333	Sphingomyelin phosphodiesterase	S375	Rho kinase	S406	RAB subfamily
S333	Neutral sphingomyelinase coupling factors	S375	Protein kinase C (PKC) family		
S334	Ceramide glucosyltransferase	S376	Alpha subfamily	<b>S412 Transporters</b>	
S334	Acid ceramidase	S376	Delta subfamily	S414	ATP-binding cassette transporter family
S334	Neutral ceramidases	S377	Eta subfamily	S415	ABCA subfamily
S335	Alkaline ceramidases	S377	Iota subfamily	S416	ABCB subfamily
S335	Ceramide kinase	S378	FRAP subfamily	S417	ABCC subfamily
S336	Chromatin modifying enzymes	S378	Cyclin-dependent kinase (CDK) family	S418	ABCD subfamily of peroxisomal ABC transporters
S336	2.1.1.- Protein arginine N-methyltransferases	S379	CDK4 subfamily	S419	ABCG subfamily
S337	3.5.1.- Histone deacetylases (HDACs)	S379	GSK subfamily	S419	F-type and V-type ATPases
S338	Cyclic nucleotide turnover/signalling	S380	Polo-like kinase (PLK) family	S420	F-type ATPase
S338	Adenylyl cyclases (ACs)	S381	STE7 family	S420	V-type ATPase
S340	Exchange protein activated by cyclic AMP (EPACs)	S382	Abl family	S420	P-type ATPases
S341	Phosphodiesterases, 3',5'-cyclic nucleotide (PDEs)	S382	Ack family	S421	P1B P-type ATPases: Cu <sup>+</sup> -ATPases
S344	Cytochrome P450	S383	Janus kinase (JAK) family	S421	P2A P-type ATPases: Ca <sup>2+</sup> -ATPases
S344	CYP1 family	S383	Src family	S422	P2B P-type ATPases: Ca <sup>2+</sup> -ATPases
S345	CYP2 family: drug metabolising subset	S384	Tec family	S422	Na <sup>+</sup> /K <sup>+</sup> -ATPases
S346	CYP2 family: physiological enzymes subset	S385	RAF family	S422	H <sup>+</sup> /K <sup>+</sup> -ATPases
S346	CYP3 family	S385	Lanosterol biosynthesis pathway	S423	P4 P-type ATPases: Phospholipid-transporting ATPases
S347	CYP4 family	S388	Nucleoside synthesis and metabolism	S423	P5 P-type ATPases: Mn <sup>2+</sup> -ATPases
S348	CYP5, CYP7 and CYP8 families	S389	Paraoxonase (PON) family	S424	SLC superfamily of solute carriers
S349	CYP11, CYP17, CYP19, CYP20 and CYP21 families	S390	Peptidases and proteinases	S425	SLC1 family of amino acid transporters
S350	CYP24, CYP26 and CYP27 families	S390	Blood coagulation components	S425	Glutamate transporter subfamily
S350	CYP39, CYP46 and CYP51 families	S391	A1: Pepsin	S427	Alanine/serine/cysteine transporter subfamily
S351	DNA topoisomerases	S391	A22: Presenilin	S427	SLC2 family of hexose and sugar alcohol transporters
S351	E3 ubiquitin ligase components	S392	C14: Caspase	S428	Class I transporters
S352	Endocannabinoid turnover	S392	M1: Aminopeptidase N	S428	Class II transporters
S353	N-Acylethanolamine turnover	S393	M2: Angiotensin-converting enzymes (ACE and ACE2)	S429	Proton-coupled inositol transporter
S354	2-Acylglycerol ester turnover			S430	SLC3 and SLC7 families of heteromeric amino acid transporters (HATs)
S355	Eicosanoid turnover	S393	M10: Matrix metalloproteinase	S430	SLC3 family
S355	Cyclooxygenase	S394	M12: Astacin/Adamalysin	S430	SLC7 family
S356	Prostaglandin synthases	S394	M28: Aminopeptidase Y	S432	SLC4 family of bicarbonate transporters
S358	Lipoxygenases	S395	M19: Membrane dipeptidase	S432	Anion exchangers
S359	Leukotriene and lipoxin metabolism	S395	S1: Chymotrypsin	S433	Sodium-dependent HCO <sub>3</sub> <sup>-</sup> transporters
S359	GABA turnover	S396	T1: Proteasome	S433	SLC5 family of sodium-dependent glucose transporters
S361	Glycerophospholipid turnover	S397	S8: Subtilisin		
S361	Phosphoinositide-specific phospholipase C	S397	S9: Prolyl oligopeptidase	S434	Hexose transporter family
S363	Phospholipase A2	S397	Peptidyl-prolyl cis/trans isomerases	S435	Choline transporter
S364	Phosphatidylcholine-specific phospholipase D	S399	Poly ADP-ribose polymerases	S436	Sodium iodide symporter, sodium-dependent multivitamin transporter and sodium-coupled monocarboxylate transporters
S365	Lipid phosphate phosphatases	S399	Prolyl hydroxylases		
S366	Phosphatidylinositol kinases	S400	Sphingosine 1-phosphate turnover	S437	Sodium myo-inositol cotransporter transporters
S368	Phosphatidylinositol phosphate kinases	S400	Sphingosine kinase	S438	SLC6 neurotransmitter transporter family
S369	Haem oxygenase	S402	Sphingosine 1-phosphate phosphatase	S439	Monoamine transporter subfamily
S370	Hydrogen sulphide synthesis	S402	Sphingosine 1-phosphate lyase	S439	GABA transporter subfamily
S371	Hydrolases	S403	Thyroid hormone turnover		
S373	Inositol phosphate turnover	S404	1.14.13.9 Kynurenine 3-monooxygenase		

S440	Glycine transporter subfamily	S466	SLC25 family of mitochondrial transporters	S487	SLC40 iron transporter
S442	Neutral amino acid transporter subfamily	S466	Mitochondrial di- and tri-carboxylic acid transporter subfamily	S488	SLC41 family of divalent cation transporters
S443	SLC8 family of sodium/calcium exchangers	S467	Mitochondrial amino acid transporter subfamily	S489	SLC42 family of Rhesus glycoprotein ammonium transporters
S444	SLC9 family of sodium/hydrogen exchangers	S468	Mitochondrial phosphate transporters	S490	SLC43 family of large neutral amino acid transporters
S444	SLC10 family of sodium-bile acid co-transporters	S468	Mitochondrial nucleotide transporter subfamily	S491	SLC44 choline transporter-like family
S445	SLC11 family of proton-coupled metal ion transporters	S469	Mitochondrial uncoupling proteins	S492	SLC45 family of putative sugar transporters
S446	SLC12 family of cation-coupled chloride transporters	S469	Miscellaneous SLC25 mitochondrial transporters	S493	SLC46 family of folate transporters
S448	SLC13 family of sodium-dependent sulphate/carboxylate transporters	S470	SLC26 family of anion exchangers	S494	SLC47 family of multidrug and toxin extrusion transporters
S449	SLC14 family of facilitative urea transporters	S470	Selective sulphate transporters	S495	SLC48 heme transporter
S450	SLC15 family of peptide transporters	S471	Chloride/bicarbonate exchangers	S495	SLC49 family of FLVCR-related heme transporters
S453	SLC16 family of monocarboxylate transporters	S471	Anion channels	S496	SLC50 sugar transporter
S454	SLC17 phosphate and organic anion transporter family	S472	Other SLC26 anion exchangers	S497	SLC51 family of steroid-derived molecule transporters
S454	Type I sodium-phosphate co-transporters	S472	SLC27 family of fatty acid transporters	S498	SLC52 family of riboflavin transporters
S455	Sialic acid transporter	S473	SLC28 and SLC29 families of nucleoside transporters	S499	SLC53 Phosphate carriers
S455	Vesicular glutamate transporters (VGLUTs)	S474	SLC28 family	S499	SLC54 Mitochondrial pyruvate carriers
S456	Vesicular nucleotide transporter	S475	SLC29 family	S500	SLC55 Mitochondrial cation/proton exchangers
S456	SLC18 family of vesicular amine transporters	S476	SLC30 zinc transporter family	S500	SLC56 Sideroflexins
S457	SLC19 family of vitamin transporters	S477	SLC31 family of copper transporters	S501	SLC57 NiPA-like magnesium transporter family
S458	SLC20 family of sodium-dependent phosphate transporters	S478	SLC32 vesicular inhibitory amino acid transporter	S501	SLC58 MagT-like magnesium transporter family
S459	SLC22 family of organic cation and anion transporters	S479	SLC33 acetylCoA transporter	S502	SLC59 Sodium-dependent lysophosphatidylcholine symporter family
S460	Organic cation transporters (OCT)	S480	SLC34 family of sodium phosphate co-transporters	S502	SLC60 Glucose transporters
S461	Organic zwitterions/cation transporters (OCTN)	S481	SLC35 family of nucleotide sugar transporters	S503	SLC61 Molybdate transporter family
S461	Organic anion transporters (OATs)	S482	SLC36 family of proton-coupled amino acid transporters	S503	SLC62 Pyrophosphate transporters
S462	Urate transporter	S483	SLC37 family of phosphosugar/phosphate exchangers	S504	SLC63 Sphingosine phosphate transporters
S463	Atypical SLC22B subfamily	S484	SLC38 family of sodium-dependent neutral amino acid transporters	S504	SLC64 Golgi Ca <sup>2+</sup> /H <sup>+</sup> exchangers
S464	SLC23 family of ascorbic acid transporters	S484	System A-like transporters	S505	SLC65 NPC-type cholesterol transporters
S465	SLC24 family of sodium/potassium/calcium exchangers	S485	System N-like transporters	S505	SLC66 Lysosomal amino acid transporters
		S485	Orphan SLC38 transporters	S506	SLCO family of organic anion transporting polypeptides
		S486	SLC39 family of metal ion transporters		

## Introduction

In order to allow clarity and consistency in pharmacology, there is a need for a comprehensive organisation and presentation of the targets of drugs. This is the philosophy of the IUPHAR/BPS Guide to PHARMACOLOGY presented on the online free access database (<http://www.guidetopharmacology.org/>). This database is supported by the British Pharmacological Society (BPS), the International Union of Basic and Clinical Pharmacology (IUPHAR), the University of Edinburgh and previously the Wellcome Trust. Data included in the Guide to PHARMACOLOGY are derived in large part from interactions with the subcommittees of the Nomenclature and Standards Committee of the International Union of Basic and Clinical Pharmacology (NC-IUPHAR). A major influence

on the development of the database was Tony Harmar (1951-2014), who worked with a passion to establish the curators as a team of highly informed and informative individuals, with a focus on high-quality data input, ensuring a suitably validated dataset. The Editors of the Concise Guide have compiled the individual records, in concert with the team of Curators, drawing on the expert knowledge of these latter subcommittees. The tables allow an indication of the status of the nomenclature for the group of targets listed, usually previously published in Pharmacological Reviews. In the absence of an established subcommittee, advice from several prominent, independent experts has generally been obtained to produce an authoritative consensus on nomenclature, which at-

tempts to fit in within the general guidelines from NC-IUPHAR. This current edition, the Concise Guide to PHARMACOLOGY 2021/22, is the latest snapshot of the database in print form, following on from the Concise Guide to PHARMACOLOGY 2019/20. It contains data drawn from the online database as a rapid overview of the major pharmacological targets. Thus, there are many fewer targets presented in the Concise Guide compared to the online database. The priority for inclusion in the Concise Guide is the presence of quantitative pharmacological data for human proteins. This means that often orphan family members are not presented in the Concise Guide, although structural information is available on the online database. The organisation of the data is tabular

(where appropriate) with a standardised format, where possible on a single page, intended to aid understanding of, and comparison within, a particular target group. The Concise Guide is intended as an initial resource, with links to additional reviews and resources for greater depth and information. Pharmacological and structural data focus primarily on human gene products, wherever possible, with links to HGNC gene nomenclature and UniProt IDs. In a few cases, where data from human proteins are limited, data from other species are indicated. Pharmacological tools listed are prioritised on the basis of selectivity and availability. That is, agents (agonists, antagonists, inhibitors, activators, etc.) are included where they

are both available (by donation or from commercial sources, now or in the near future) AND the most selective. The Concise Guide is divided into seven sections, which comprise pharmacological targets of similar structure/function. These are G protein-coupled receptors, ion channels (combining previous records of ligand-gated, voltage-gated and other ion channels), catalytic receptors, nuclear hormone receptors, enzymes, transporters and other protein targets. We hope that the Concise Guide will provide for researchers, teachers and students a state-of-the art source of accurate, curated information on the background to their work that they will use in the Introductions to their Research Papers or Reviews, or in sup-

porting their teaching and studies. We recommend that any citations to information in the Concise Guide are presented in the following format:

Alexander SPH *et al.* (2021). The Concise Guide to PHARMACOLOGY 2021/22: Overview. *Br J Pharmacol* 178: S1–S26.

In this overview are listed protein targets of pharmacological interest, which are not G protein-coupled receptors, ion channels, nuclear hormone receptors, catalytic receptors, transporters or enzymes. For obvious reasons, we have included potential drug targets of the SARS-CoV-2 virus, despite the current limited pharmacological data.

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### Conflict of interest

The authors state that there are no conflicts of interest to disclose.

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## Family structure

–	Abscisic acid receptor complex	–	Hypoxia-inducible factors	S18	R4 family
S8	Adiponectin receptors	–	Immune checkpoint proteins	S19	R7 family
–	Anti-infective targets	–	Immunoglobulin C1-set domain-containing proteins	S19	R12 family
–	Antimalarial targets	–	Immunoglobulin C2-set domain-containing proteins	–	Repulsive guidance molecules
–	Other anti-infective targets	–	Immunoglobulin like domain containing proteins	–	Reticulons and associated proteins
S9	Aryl hydrocarbon receptor	–	Immunoglobulins	–	Ribosomal factors
–	B-cell lymphoma 2 (Bcl-2) protein family	–	Inhibitors of apoptosis (IAP) protein family	–	Sialic acid binding Ig like lectins
–	Bromodomain-containing proteins	–	Kelch-like proteins	S20	Sigma receptors
S10	Non-enzymatic BRD containing proteins	–	Kinesins	–	Signal regulatory proteins
–	Butyrophilin and butyrophilin-like proteins	–	Leucine-rich repeat proteins	–	Tetraspanins
S11	CD molecules	–	Lymphocyte antigens	–	Transcription factors
–	Chaperone proteins	–	Mitochondrial-associated proteins	–	Transcription factor regulators
–	Lipid binding chaperones	–	Myosin binding proteins	–	NF-κB regulators
–	Chitinase-like proteins	–	Neuropilins and Plexins	S21	Transthyretin
–	Chromatin-interacting transcriptional repressors	–	Non-catalytic pattern recognition receptors	S22	Tubulins
S13	Methyllysine reader proteins	–	Notch receptors	–	Tumour-associated antigens
–	Circadian clock proteins	–	Nuclear export proteins	–	WD repeat-containing proteins
–	Claudins	–	Pentraxins	–	Plasmodium multidrug resistance family
–	Cytolytic pore-forming proteins	S16	Regulators of G protein Signaling (RGS) proteins	S23	SARS-CoV-2
–	EF-hand domain containing proteins	–	RZ family	S23	Structural proteins
S14	Fatty acid-binding proteins	–		S24	Polyproteins
–	Guanine nucleotide exchange factors (GEFs)	S17		S24	Proteases
–	Heat shock proteins	S17		S25	Nucleic acid turnover
				S25	Other proteins



# Adiponectin receptors

Other protein targets → Adiponectin receptors

**Overview:** Adiponectin receptors (**provisional nomenclature**, [ENSM00500000270960](#)) respond to the 30 kDa complement-related protein hormone adiponectin (also known as [ADIPOQ](#); adipocyte, C1q and collagen domain-containing protein; ACRP30, adipose most abundant

gene transcript 1; apM-1; gelatin-binding protein: [Q15848](#)) originally cloned from adipocytes [69]. Although sequence data suggest 7TM domains, immunological evidence indicates that, contrary to typical 7TM topology, the carboxyl terminus is extracellular, while the amino terminus is intracellular [136].

Signalling through these receptors appears to avoid G proteins; modelling based on the crystal structures of the adiponectin receptors suggested ceramidase activity, which would make these the first in a new family of catalytic receptors [121].

## Further reading on Adiponectin receptors

Fisman EZ *et al.* (2014) Adiponectin: a manifold therapeutic target for metabolic syndrome, diabetes, and coronary disease? *Cardiovasc Diabetol* **13**: 103 [[PMID:24957699](#)]  
 Okada-Iwabu M *et al.* (2018) Structure and function analysis of adiponectin receptors toward development of novel antidiabetic agents promoting healthy longevity. *Endocr J* **65**: 971-977 [[PMID:30282888](#)]  
 Ruan H *et al.* (2016) Adiponectin signaling and function in insulin target tissues. *J Mol Cell Biol* **8**: 101-9 [[PMID:26993044](#)]

Wang Y *et al.* (2017) Cardiovascular Adiponectin Resistance: The Critical Role of Adiponectin Receptor Modification. *Trends Endocrinol Metab* **28**: 519-530 [[PMID:28473178](#)]  
 Zhao L *et al.* (2014) Adiponectin and insulin cross talk: the microvascular connection. *Trends Cardiovasc Med* **24**: 319-24 [[PMID:25220977](#)]

Nomenclature	<a href="#">Adipo1 receptor</a>	<a href="#">Adipo2 receptor</a>
HGNC, UniProt	<a href="#">ADIPOR1</a> , <a href="#">Q96A54</a>	<a href="#">ADIPOR2</a> , <a href="#">Q86V24</a>
Rank order of potency	globular adiponectin ( <a href="#">ADIPOQ</a> , <a href="#">Q15848</a> ) > adiponectin ( <a href="#">ADIPOQ</a> , <a href="#">Q15848</a> )	globular adiponectin ( <a href="#">ADIPOQ</a> , <a href="#">Q15848</a> ) = adiponectin ( <a href="#">ADIPOQ</a> , <a href="#">Q15848</a> )

**Comments:** T-Cadherin ([CDH13](#), [P55290](#)) has also been suggested to be a receptor for (hexameric) adiponectin [47].

# Aryl hydrocarbon receptor

Other protein targets → [Aryl hydrocarbon receptor](#)

**Overview:** The aryl hydrocarbon receptor, highly expressed in the liver and barrier organs, is resident in the cytoplasm bound to the chaperone heat shock protein hsp90. Upon agonist activation, the ligand:aryl hydrocarbon receptor complex

migrates to the nucleus and binds the aryl hydrocarbon receptor nuclear translocator ([ARNT](#), [P27540](#), also known as HIF1 $\beta$ ). The complex regulates transcription of selected genes through interaction with xenobiotic response elements (XRE). Among the

genes regulated by the AHR/ARNT complex are cytochrome P450s, particularly CYP1A1, and the period circadian protein homolog 1 ([PER1](#), [O15534](#)). The aryl hydrocarbon receptor is also capable of non-genomic signalling.

## Further reading on Aryl hydrocarbon receptor

Bock KW. (2019) Aryl hydrocarbon receptor (AHR): From selected human target genes and crosstalk with transcription factors to multiple AHR functions. *Biochem Pharmacol* **168**: 65-70 [[PMID:31228464](#)]

Bock KW. (2020) Aryl hydrocarbon receptor (AHR) functions: Balancing opposing processes including inflammatory reactions. *Biochem Pharmacol* **178**: 114093 [[PMID:32535108](#)]

Esser C *et al.* (2015) The aryl hydrocarbon receptor in barrier organ physiology, immunology, and toxicology. *Pharmacol Rev* **67**: 259-79 [[PMID:25657351](#)]

Roman AC *et al.* (2018) The aryl hydrocarbon receptor in the crossroad of signalling networks with therapeutic value. *Pharmacol Ther* **185**: 50-63 [[PMID:29258844](#)]

Rothhammer V *et al.* (2019) The aryl hydrocarbon receptor: an environmental sensor integrating immune responses in health and disease. *Nat Rev Immunol* **19**: 184-197 [[PMID:30718831](#)]

Shi Y *et al.* (2020) The aryl hydrocarbon receptor: An environmental effector in the pathogenesis of fibrosis. *Pharmacol Res* **160**: 105180 [[PMID:32877693](#)]

Nomenclature

HGNC, UniProt

Agonists

Antagonists

[Aryl hydrocarbon receptor](#)

[AHR](#), [P35869](#)

[indolo\[3,2-b\]carbazole](#) [[12](#)] – Mouse, [tapinarof](#) [[110](#)], [indole-3-carbinol](#) [[12](#)] – Mouse, [TCDD](#)

[ezutromid](#) (pK<sub>d</sub> 7.3) [[132](#)]

## Non-enzymatic BRD containing proteins

Other protein targets → Bromodomain-containing proteins → Non-enzymatic BRD containing proteins

**Overview:** Bromodomains bind proteins with acetylated lysine residues, such as histones, to regulate gene transcription. Listed herein are examples of bromodomain-containing proteins for which sufficient pharmacology exists.

### Further reading on Non-enzymatic BRD containing proteins

Fujisawa T *et al.* (2017) Functions of bromodomain-containing proteins and their roles in homeostasis and cancer. *Nat Rev Mol Cell Biol* **18**: 246-262 [PMID:28053347]

Myrianthopoulos V *et al.* (2019) From bench to bedside, via desktop. Recent advances in the application of cutting-edge in silico tools in the research of drugs targeting bromodomain modules. *Biochem Pharmacol* **159**: 40-51 [PMID:30414936]

Nicholas DA *et al.* (2017) BET bromodomain proteins and epigenetic regulation of inflammation: implications for type 2 diabetes and breast cancer. *Cell Mol Life Sci* **74**: 231-243 [PMID:27491296]

Ramadoss M *et al.* (2018) Targeting the cancer epigenome: synergistic therapy with bromodomain inhibitors. *Drug Discov Today* **23**: 76-89 [PMID:28943305]

Spriano F *et al.* (2020) Targeting BET bromodomain proteins in cancer: The example of lymphomas. *Pharmacol Ther* **215**: 107631 [PMID:32693114]

Tang P *et al.* (2021) Targeting Bromodomain and Extraterminal Proteins for Drug Discovery: From Current Progress to Technological Development. *J Med Chem* **64**: 2419-2435 [PMID:33616410]

Nomenclature	bromodomain adjacent to zinc finger domain 2A	bromodomain adjacent to zinc finger domain 2B	CREB binding protein	polybromo 1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4
HGNC, UniProt	BAZ2A, Q9UIF9	BAZ2B, Q9UIF8	CREBBP, Q92793	PBRM1, Q86U86	SMARCA4, P51532
Selective inhibitors	GSK2801 (pK <sub>d</sub> 6.6) [87]	GSK2801 (Binding) (pK <sub>d</sub> 6.9) [87]	I-CBP112 (pK <sub>d</sub> 6.8) [88]	PFI-3 (Binding) (pK <sub>d</sub> 7.3) [101]	PFI-3 (Binding) (pK <sub>d</sub> 7.1) [101]

# CD molecules

Other protein targets → CD molecules

**Overview:** Cluster of differentiation refers to an attempt to catalogue systematically a series of over 300 cell-surface proteins associated with immunotyping. Many members of the group have identified functions as enzymes (for example, see [CD73](#)

[ecto-5'-nucleotidase](#)) or receptors (for example, see [CD41 integrin, alpha 2b subunit](#)). Many CDs are targeted for therapeutic gain using antibodies for the treatment of proliferative disorders. A full listing of all the Clusters of

Differentiation proteins is not possible in the Guide to PHARMACOLOGY; listed herein are selected members of the family targeted for therapeutic gain.

## Further reading on CD molecules

Bewersdorf JP *et al.* (2021) Immune checkpoint inhibition in myeloid malignancies: Moving beyond the PD-1/PD-L1 and CTLA-4 pathways. *Blood Rev* **45**: 100709 [[PMID:32487480](#)]  
Chi Z *et al.* (2021) Transcriptional and epigenetic regulation of PD-1 expression. *Cell Mol Life Sci* **78**: 3239-3246 [[PMID:33738533](#)]  
Gabius HJ *et al.* (2015) The glycobiology of the CD system: a dictionary for translating marker designations into glycan/lectin structure and function. *Trends Biochem Sci* **40**: 360-76 [[PMID:25981696](#)]

Huang MY *et al.* (2021) Combination therapy with PD-1/PD-L1 blockade in non-small cell lung cancer: strategies and mechanisms. *Pharmacol Ther* **219**: 107694 [[PMID:32980443](#)]  
Vosoughi T *et al.* (2019) CD markers variations in chronic lymphocytic leukemia: New insights into prognosis. *J Cell Physiol* **234**: 19420-19439 [[PMID:31049958](#)]

Nomenclature	CD2	CD3e	CD6	CD20 (membrane-spanning 4-domains, subfamily A, member 1)	CD33
Common abbreviation	–	–	–	–	SIGLEC3
HGNC, UniProt	<a href="#">CD2</a> , <a href="#">P06729</a>	<a href="#">CD3E</a> , <a href="#">P07766</a>	<a href="#">CD6</a> , <a href="#">P30203</a>	<a href="#">MS4A1</a> , <a href="#">P11836</a>	<a href="#">CD33</a> , <a href="#">P20138</a>
Selective inhibitors	<a href="#">alefacept</a> [ <a href="#">23</a> , <a href="#">74</a> ]	–	–	–	–
Antibodies	–	<a href="#">catumaxomab</a> (Binding) [ <a href="#">63</a> ], <a href="#">muromonab-CD3</a> (Binding) [ <a href="#">32</a> ], <a href="#">otelixizumab</a> (Binding) [ <a href="#">14</a> ]	–	<a href="#">ofatumumab</a> (Binding) ( $pK_d$ 9.9) [ <a href="#">58</a> ], <a href="#">rituximab</a> (Binding) ( $pK_d$ 8.5) [ <a href="#">113</a> ], <a href="#">ibritumomab tiuxetan</a> (Binding), <a href="#">obinutuzumab</a> (Binding) [ <a href="#">3</a> , <a href="#">90</a> ], <a href="#">tositumomab</a> (Binding)	<a href="#">lintuzumab</a> (Binding) ( $pK_d$ ~10) [ <a href="#">16</a> ], <a href="#">gemtuzumab ozogamicin</a> (Binding) [ <a href="#">10</a> ]

Nomenclature	CD52	CD80	CD86	cytotoxic T-lymphocyte-associated protein 4 (CD152)	programmed cell death 1 (CD279)	CD300a
Common abbreviation	–	–	–	CTLA-4	PD-1	–
HGNC, UniProt	<a href="#">CD52</a> , <a href="#">P31358</a>	<a href="#">CD80</a> , <a href="#">P33681</a>	<a href="#">CD86</a> , <a href="#">P42081</a>	<a href="#">CTLA4</a> , <a href="#">P16410</a>	<a href="#">PDCD1</a> , <a href="#">Q15116</a>	<a href="#">CD300A</a> , <a href="#">Q9UGN4</a>
Endogenous ligands	–	–	–	–	<a href="#">programmed cell death 1 ligand 1 (CD274, Q9NZQ7)</a> (Binding)	–
Selective inhibitors	–	<a href="#">abatacept</a> ( $pK_d \sim 7.9$ ) <a href="#">[64, 125]</a>	<a href="#">abatacept</a> ( $pK_d \sim 7.9$ ) <a href="#">[64, 125]</a> , <a href="#">belatacept</a> <a href="#">[57]</a>	–	–	–
Antibodies	<a href="#">alemtuzumab</a> (Binding) <a href="#">[30, 89]</a>	–	–	<a href="#">ipilimumab</a> (Binding) ( $pK_d$ >9) <a href="#">[33]</a> , <a href="#">tremelimumab</a> (Binding) ( $pK_d$ 8.9) <a href="#">[35]</a>	<a href="#">pembrolizumab</a> (Binding) ( $pK_d \sim 10$ ) <a href="#">[17]</a> , <a href="#">nivolumab</a> (Binding) ( $pK_d$ 9.1) <a href="#">[38, 54, 49]</a>	–

**Comments:** The endogenous ligands for human PD-1 are programmed cell death 1 ligand 1 (PD-L1 *aka* [CD274](#) ([CD274](#), [Q9NZQ7](#))) and programmed cell death 1 ligand 2 (PD-L2; [PDCD1LG2](#)). These ligands are cell surface peptides, normally involved in immune system regulation. Expression of PD-1 by cancer cells induces immune tolerance and evasion of immune system attack. Anti-PD-1 monoclonal antibodies are used to induce immune checkpoint blockade as a therapeutic intervention in cancer, effectively re-establishing immune vigilance. [Pembrolizumab](#) was the first anti-PD-1 antibody to be approved by the US FDA.

# Methyllysine reader proteins

Other protein targets → Chromatin-interacting transcriptional repressors → Methyllysine reader proteins

**Overview:** Methyllysine reader proteins bind to methylated proteins, such as histones, allowing regulation of gene expression.

## Further reading on Methyllysine reader proteins

Daskalaki MG *et al.* (2018) Histone methylation and acetylation in macrophages as a mechanism for regulation of inflammatory responses. *J Cell Physiol* **233**: 6495-6507 [PMID:29574768]  
Furuya K *et al.* (2019) Epigenetic interplays between DNA demethylation and histone methylation for protecting oncogenesis. *J Biochem* **165**: 297-299 [PMID:30605533]  
Levy D. (2019) Lysine methylation signaling of non-histone proteins in the nucleus. *Cell Mol Life Sci* **76**: 2873-2883 [PMID:31123776]

Li J *et al.* (2019) Understanding histone H3 lysine 36 methylation and its deregulation in disease. *Cell Mol Life Sci* **76**: 2899-2916 [PMID:31147750]  
Shafabakhsh R *et al.* (2019) Role of histone modification and DNA methylation in signaling pathways involved in diabetic retinopathy. *J Cell Physiol* **234**: 7839-7846 [PMID:30515789]

Nomenclature

L3MBTL histone methyl-lysine binding protein 3

HGNC, UniProt

L3MBTL3, Q96JM7

Selective agonists

UNC1215 [50]

# Fatty acid-binding proteins

Other protein targets → **Fatty acid-binding proteins**

**Overview:** Fatty acid-binding proteins are low molecular weight (100-130 aa) chaperones for long chain fatty acids, fatty acyl CoA esters, eicosanoids, retinols, retinoic acids and related metabolites and are usually regarded as being responsible for

allowing the otherwise hydrophobic ligands to be mobile in aqueous media. These binding proteins may perform functions extracellularly (*e.g.* in plasma) or transport these agents; to the nucleus to interact with nuclear receptors (principally PPARs and

retinoic acid receptors [99]) or for interaction with metabolic enzymes. Although sequence homology is limited, crystallographic studies suggest conserved 3D structures across the group of binding proteins.

## Further reading on Fatty acid-binding proteins

Gajda AM *et al.* (2015) Enterocyte fatty acid-binding proteins (FABPs): different functions of liver and intestinal FABPs in the intestine. *Prostaglandins Leukot Essent Fatty Acids* **93**: 9-16 [PMID:25458898]

Glatz JF. (2015) Lipids and lipid binding proteins: a perfect match. *Prostaglandins Leukot Essent Fatty Acids* **93**: 45-9 [PMID:25154384]

Hotamisligil GS *et al.* (2015) Metabolic functions of FABPs—mechanisms and therapeutic implications. *Nat Rev Endocrinol* **11**: 592-605 [PMID:26260145]

Matsumata M *et al.* (2016) Fatty acid binding proteins and the nervous system: Their impact on mental conditions. *Neurosci Res* **102**: 47-55 [PMID:25205626]

Nguyen HC *et al.* (2020) Role of the Fatty Acid Binding Proteins in Cardiovascular Diseases: A Systematic Review. *J Clin Med* **9**: [PMID:33105856]

Osumi T *et al.* (2016) Heart lipid droplets and lipid droplet-binding proteins: Biochemistry, physiology, and pathology. *Exp Cell Res* **340**: 198-204 [PMID:26524506]

Nomenclature	fatty acid binding protein 1	fatty acid binding protein 2	fatty acid binding protein 3	fatty acid binding protein 4	fatty acid binding protein 5
HGNC, UniProt	<i>FABP1</i> , P07148	<i>FABP2</i> , P12104	<i>FABP3</i> , P05413	<i>FABP4</i> , P15090	<i>FABP5</i> , Q01469
Rank order of potency	stearic acid, oleic acid > palmitic acid, linoleic acid > arachidonic acid, $\alpha$ -linolenic acid [91]	stearic acid > palmitic acid, oleic acid > linoleic acid > arachidonic acid, $\alpha$ -linolenic acid [91]	stearic acid, oleic acid, palmitic acid > linoleic acid, $\alpha$ -linolenic acid, arachidonic acid [91]	oleic acid, palmitic acid, stearic acid, linoleic acid > $\alpha$ -linolenic acid, arachidonic acid [91]	–
Inhibitors	fenofibrate (pK <sub>i</sub> 7.6) [18] – Rat, fenofibric acid (pK <sub>i</sub> 6.5) [18] – Rat, HTS01037 (pK <sub>i</sub> 5.1) [42] – Mouse	–	–	–	compound 13 (pK <sub>i</sub> 8.7) [118]
Selective inhibitors	–	–	–	HM50316 (pK <sub>i</sub> >9) [66]	–
Comments	A broader substrate specificity than other FABPs, binding two fatty acids per protein [123].	Crystal structure of the rat FABP2 [95].	Crystal structure of the human FABP3 [137].	–	Crystal structure of the human FABP5 [44].



Nomenclature	<a href="#">fatty acid binding protein 6</a>	<a href="#">fatty acid binding protein 7</a>	<a href="#">peripheral myelin protein 2</a>	<a href="#">fatty acid binding protein 9</a>	<a href="#">fatty acid binding protein 12</a>
HGNC, UniProt	<a href="#">FABP6, P51161</a>	<a href="#">FABP7, O15540</a>	<a href="#">PMP2, P02689</a>	<a href="#">FABP9, Q0Z7S8</a>	<a href="#">FABP12, A6NFH5</a>
Comments	Able to transport bile acids [142].	Crystal structure of the human FABP7 [9].	<i>In silico</i> modelling suggests that PMP2/FABP8 can bind both fatty acids and cholesterol [70].	–	–

  

Nomenclature	<a href="#">retinol binding protein 1</a>	<a href="#">retinol binding protein 2</a>	<a href="#">retinol binding protein 3</a>	<a href="#">retinol binding protein 4</a>	<a href="#">retinol binding protein 5</a>	<a href="#">retinol binding protein 7</a>
HGNC, UniProt	<a href="#">RBP1, P09455</a>	<a href="#">RBP2, P50120</a>	<a href="#">RBP3, P10745</a>	<a href="#">RBP4, P02753</a>	<a href="#">RBP5, P82980</a>	<a href="#">RBP7, Q96R05</a>
Rank order of potency	–	stearic acid > palmitic acid, oleic acid, linoleic acid, $\alpha$ -linolenic acid, arachidonic acid [92]	–	–	–	–
Inhibitors	–	–	–	A1120 (pIC <sub>50</sub> 7.8) [128]	–	–

  

Nomenclature	<a href="#">retinaldehyde binding protein 1</a>	<a href="#">cellular retinoic acid binding protein 1</a>	<a href="#">cellular retinoic acid binding protein 2</a>
HGNC, UniProt	<a href="#">RLBP1, P12271</a>	<a href="#">CRABP1, P29762</a>	<a href="#">CRABP2, P29373</a>
Rank order of potency	11- <i>cis</i> -retinal, 11- <i>cis</i> -retinol > 9- <i>cis</i> -retinal, 13- <i>cis</i> -retinal, 13- <i>cis</i> -retinol, all- <i>trans</i> -retinal, retinol [22]	tretinoin > alitretinoin stearic acid > palmitic acid, oleic acid, linoleic acid, $\alpha$ -linolenic acid, arachidonic acid [92]	–

**Comments:** Although not tested at all FABPs, [BMS309403](#) exhibits high affinity for FABP4 (pIC<sub>50</sub> 8.8) compared to FABP3 or FABP5 (pIC<sub>50</sub> <6.6) [27, 118]. [HTS01037](#) is reported to interfere with FABP4 action [42]. Ibuprofen displays some selectivity for FABP4 (pIC<sub>50</sub> 5.5) relative to FABP3 (pIC<sub>50</sub> 3.5) and FABP5 (pIC<sub>50</sub> 3.8) [68]. Fenofibric acid displays some selectivity for FABP5 (pIC<sub>50</sub> 5.5) relative to FABP3 (pIC<sub>50</sub> 4.5) and FABP4 (pIC<sub>50</sub> 4.6) [68]. Multiple pseudogenes for the FABPs have been identified in the human genome.

# Notch receptors

Other protein targets → Notch receptors

**Overview:** Aberrant Notch signalling is implicated in a number of human cancers [59, 80, 108, 126], and there is intense pharmaceutical activity being directed towards achieving clinically effective Notch pathway inhibition [24, 75].

## Further reading on Notch receptors

Fabbro D *et al.* (2020) Notch Inhibition in Cancer: Challenges and Opportunities. *Chimia (Aarau)*

**74:** 779-783 [PMID:33115560]

Moore G *et al.* (2020) Top Notch Targeting Strategies in Cancer: A Detailed Overview of Recent Insights and Current Perspectives. *Cells* **9:** [PMID:32575680]

Palmer WH *et al.* (2015) Ligand-Independent Mechanisms of Notch Activity. *Trends Cell Biol* **25:** 697-707 [PMID:26437585]

Previs RA *et al.* (2015) Molecular pathways: translational and therapeutic implications of the Notch signaling pathway in cancer. *Clin Cancer Res* **21:** 955-61 [PMID:25388163]

Takebe N *et al.* (2015) Targeting Notch, Hedgehog, and Wnt pathways in cancer stem cells: clinical update. *Nat Rev Clin Oncol* **12:** 445-64 [PMID:25850553]

Nomenclature	notch receptor 1	notch receptor 2	notch receptor 3	notch receptor 4
HGNC, UniProt	NOTCH1, P46531	NOTCH2, Q04721	NOTCH3, Q9UM47	NOTCH4, Q99466
Inhibitors	IMR-1 (Binding) (pK <sub>d</sub> 5) [8]	–	–	–
Antibodies	brontictuzumab (Binding) (pK <sub>d</sub> 8.4) [30]	tarextumab (Binding) (pK <sub>d</sub> >10) [31]	tarextumab (Binding) (pK <sub>d</sub> 9.9) [31]	–
Comments	Various types of activating and inactivating NOTCH1 mutations have been reported to be associated with human diseases, for example: aortic valve disease [29, 73], Adams-Oliver syndrome 5 [114], T-cell acute lymphoblastic leukemia (T-ALL) [130], chronic lymphocytic leukemia (CLL) [89] and head and neck squamous cell carcinoma [1, 115].	–	–	Notch receptor 4 is a potential therapeutic molecular target for triple-negative breast cancer [60, 77].

# Regulators of G protein Signaling (RGS) proteins

Other protein targets → Regulators of G protein Signaling (RGS) proteins

**Overview:** Regulator of G protein Signaling, or RGS, proteins serve an important regulatory role in signaling mediated by G protein-coupled receptors (GPCRs). They all share a common RGS domain that directly interacts with active, GTP-bound  $G\alpha$  subunits of heterotrimeric G proteins. RGS proteins stabilize the transition state for GTP hydrolysis on  $G\alpha$  and thus induce a

conformational change in the  $G\alpha$  subunit that accelerates GTP hydrolysis, thereby effectively turning off signaling cascades mediated by GPCRs. This GTPase accelerating protein (GAP) activity is the canonical mechanism of action for RGS proteins, although many also possess additional functions and domains. RGS proteins are divided into four families, R4, R7, R12 and RZ

based on sequence homology, domain structure as well as specificity towards  $G\alpha$  subunits. For reviews on RGS proteins and their potential as therapeutic targets, see *e.g.* [5, 45, 79, 93, 105, 106, 107, 138, 140].

## Further reading on Regulators of G protein Signaling (RGS) proteins

Alqinyah M *et al.* (2018) Regulating the regulators: Epigenetic, transcriptional, and post-translational regulation of RGS proteins. *Cell Signal* **42**: 77-87 [PMID:29042285]  
 Fuentes N *et al.* (2021) RGS proteins, GRKs, and beta-arrestins modulate G protein-mediated signaling pathways in asthma. *Pharmacol Ther* **223**: 107818 [PMID:33600853]  
 Neubig RR *et al.* (2002) Regulators of G-protein signalling as new central nervous system drug targets. *Nat Rev Drug Discov* **1**: 187-97 [PMID:12120503]

Sethakorn N *et al.* (2010) Non-canonical functions of RGS proteins. *Cell Signal* **22**: 1274-81 [PMID:20363320]  
 Sjögren B. (2017) The evolution of regulators of G protein signalling proteins as drug targets - 20 years in the making: IUPHAR Review 21. *Br J Pharmacol* **174**: 427-437 [PMID:28098342]  
 Sjögren B *et al.* (2010) Thinking outside of the "RGS box": new approaches to therapeutic targeting of regulators of G protein signaling. *Mol Pharmacol* **78**: 550-7 [PMID:20664002]

## RZ family

Other protein targets → Regulators of G protein Signaling (RGS) proteins → RZ family

**Overview:** The RZ family of RGS proteins is less well characterized than the other families. It consists of, RGS17 (also known as RGSZ2), RGS19 (also known as GAIP) and RGS20 (with several splice variants including RGSZ1 and Ret-RGS). All members contain an N-terminal cysteine string motif [62] which

is a site of palmitoylation and could serve functions in membrane targeting, protein stability or aid protein-protein interactions [2, 62]. However, the function in the case of RZ family RGS proteins is not yet fully understood. Members of the RZ family of RGS proteins are the only RGS proteins that have

selective GAP activity for  $G\alpha_z$ , a function that resulted in the name of the family [31, 71, 127, 134]. However, the members of the RZ family are able to also GAP  $G\alpha_{i/o}$  members with varying selectivity.

Nomenclature	regulator of G-protein signaling 17	regulator of G-protein signaling 19	regulator of G-protein signaling 20
Common abbreviation	RGS17	RGS19	RGS20
HGNC, UniProt	RGS17, Q9UGC6	RGS19, P49795	RGS20, O76081

## R4 family

Other protein targets → Regulators of G protein Signaling (RGS) proteins → R4 family

**Overview:** The R4 family of RGS proteins is the largest family of RGS proteins with 10 members. Each of the R4 family members contain only small N- and C-termini apart from the RGS domain. The N-terminal amphipathic helix present in most R4 family

members serves an important function in membrane association and can directly bind phospholipids. In contrast to the RGS domain, which is well conserved among members of the R4 family of RGS proteins, the N- and C-termini vary, enabling

specificity of non-GAP functions. Despite the non-complex structure of these proteins, several R4 family RGS proteins have been shown to possess additional functions apart from acting as GAPs at activated G $\alpha$  subunits [11, 96].

### Further reading on R4 family

Xie Z *et al.* (2016) R4 Regulator of G Protein Signaling (RGS) Proteins in Inflammation and Immunity. *AAPS J* **18**: 294-304 [PMID:26597290]

Nomenclature	regulator of G-protein signaling 1	regulator of G-protein signaling 2	regulator of G-protein signaling 3	regulator of G-protein signaling 4
Common abbreviation	RGS1	RGS2	RGS3	RGS4
HGNC, UniProt	<a href="#">RGS1</a> , <a href="#">Q08116</a>	<a href="#">RGS2</a> , <a href="#">P41220</a>	<a href="#">RGS3</a> , <a href="#">P49796</a>	<a href="#">RGS4</a> , <a href="#">P49798</a>
Selective inhibitors	–	–	–	<a href="#">RGS4 inhibitor 11b</a> (pIC <sub>50</sub> 7.8) [124], <a href="#">CCG-50014</a> (pIC <sub>50</sub> 7.5) [13, 124], <a href="#">RGS4 inhibitor 13</a> (pIC <sub>50</sub> 7.3) [124]

  

Nomenclature	regulator of G-protein signaling 5	regulator of G-protein signaling 8	regulator of G-protein signaling 13	regulator of G-protein signaling 16	regulator of G-protein signaling 18	regulator of G-protein signaling 21
Common abbreviation	RGS5	RGS8	RGS13	RGS16	RGS18	RGS21
HGNC, UniProt	<a href="#">RGS5</a> , <a href="#">O15539</a>	<a href="#">RGS8</a> , <a href="#">P57771</a>	<a href="#">RGS13</a> , <a href="#">O14921</a>	<a href="#">RGS16</a> , <a href="#">O15492</a>	<a href="#">RGS18</a> , <a href="#">Q9NS28</a>	<a href="#">RGS21</a> , <a href="#">Q2M5E4</a>

## R7 family

Other protein targets → Regulators of G protein Signaling (RGS) proteins → R7 family

**Overview:** The members of the R7 family of RGS proteins [6] are more complex structures than the R4 family and are closely related to the *C. elegans* homologues EGL-10 and EAT-16 that were identified in the early stage of RGS protein research [36, 55]. Apart from the RGS domain, several additional domains are

present in these proteins that mediate protein-protein interactions, sub-cellular localization and protein stability. All R7 family members form obligatory dimers with Gβ5 through the G-γ like (GGL) domain and the disheveled-EGL10-Pleckstrin homology (DEP) domain [109]. The DEP and DEP helical

extension domain interact with R7 binding protein (R7BP) or RGS9 anchoring protein (R9AP; in retina) that serves as a plasma membrane anchoring mechanism [41, 51].

Nomenclature	regulator of G-protein signaling 6	regulator of G-protein signaling 7	regulator of G-protein signaling 9	regulator of G-protein signaling 11
Common abbreviation	RGS6	RGS7	RGS9	RGS11
HGNC, UniProt	RGS6, P49758	RGS7, P49802	RGS9, O75916	RGS11, O94810

## R12 family

Other protein targets → Regulators of G protein Signaling (RGS) proteins → R12 family

**Overview:** The R12 family consisting of RGS10, 12 and 14. RGS12 and 14 are large proteins with additional domains that can participate in protein-protein interactions and other functions. In contrast, RGS10 is a small protein consisting of the RGS domain and small N- and C-termini, similar to members of

the R4 family. However, the sequence homology the RGS10 RGS domain clearly places it in the R12 family [58]. The Gα<sub>i/o</sub>-Loco (GoLoco) motif in RGS12 and 14 has GDI activity (for Guanine nucleotide Dissociation Inhibitor) towards Gα<sub>i1</sub>, Gα<sub>i2</sub> and Gα<sub>i3</sub> [53, 105]. Through this activity RGS12 and RGS14 can inhibit G

protein signaling both by accelerating GTP hydrolysis and by preventing G protein activation. Splice variants of RGS12 and RGS14 also contain membrane targeting and protein-protein interaction domains [97, 111, 112].

Nomenclature	regulator of G-protein signaling 10	regulator of G-protein signaling 12	regulator of G-protein signaling 14
Common abbreviation	RGS10	RGS12	RGS14
HGNC, UniProt	RGS10, O43665	RGS12, O14924	RGS14, O43566

# Sigma receptors

Other protein targets → **Sigma receptors**

**Overview:** Although termed 'receptors', the evidence for coupling through conventional signalling pathways is lacking. Initially described as a subtype of opioid receptors, there is only a modest pharmacological overlap and no structural convergence with the G protein-coupled receptors; the crystal structure of the sigma1 receptor [98] suggests a trimeric structure of a single short transmembrane domain traversing the endoplasmic reticulum membrane, with the bulk of the protein facing the cytosol. A wide range of compounds, ranging from psychoactive agents to antihistamines, have been observed to bind to these sites.

## Further reading on Sigma receptors

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Nomenclature	sigma non-opioid intracellular receptor 1	$\sigma 2$
HGNC, UniProt	<i>SIGMAR1</i> , Q99720	<i>TMEM97</i> , Q5BJF2
Agonists	–	1,3-ditolylguanidine [61] – Guinea pig
Selective agonists	PRE-084 [117], (+)-SKF 10.047	–
Antagonists	–	SM 21 (pIC <sub>50</sub> 7.2) [67]
Selective antagonists	NE-100 (pIC <sub>50</sub> 8.4) [81], BD-1047 (pIC <sub>50</sub> 7.4) [72]	–
Labelled ligands	[ <sup>3</sup> H]pentazocine (Agonist)	[ <sup>3</sup> H]-di-o-tolylguanidine (Agonist)
Comments	–	The sigma2 receptor has been reported to be TMEM97 [4], a 4TM protein partner of NPC1, the Niemann-Pick C1 protein, a 13TM cholesterol-binding protein.

**Comments:** (-)-pentazocine also shows activity at opioid receptors. The sigma2 receptor has recently been reported to be TMEM97 [4], a 4TM protein partner of NPC1, the Niemann-Pick C1 protein, a 13TM cholesterol-binding protein.

# Transthyretin

Other protein targets → [Transthyretin](#)

**Overview:** Transthyretin (TTR) is a homo-tetrameric protein which transports thyroxine in the plasma and cerebrospinal fluid and retinol (vitamin A) in the plasma. Many disease causing mutations in the protein have been reported, many of which cause complex dissociation and protein mis-assembly and deposition of toxic aggregates amyloid fibril formation [84].

These amyloidogenic mutants are linked to the development of pathological amyloidoses, including familial amyloid polyneuropathy (FAP) [7, 20], familial amyloid cardiomyopathy (FAC) [49], amyloidotic vitreous opacities, carpal tunnel syndrome [76] and others. In old age, non-mutated TTR can also form pathological amyloid fibrils [131]. Pharmacological

intervention to reduce or prevent TTR dissociation is being pursued as a therapeutic strategy. To date one small molecule kinetic stabilising molecule ([tafamidis](#)) has been approved for FAP, and is being evaluated in clinical trials for other TTR amyloidoses.

## Further reading on Transthyretin

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Nomenclature

[transthyretin](#)

Common abbreviation

TTR

HGNC, UniProt

[TTR](#), [P02766](#)

Inhibitors

[tafamidis](#) (pK<sub>d</sub> 8.7) [15]

**Comments:** Excess production and accumulation of TTR causes hereditary transthyretin-mediated amyloidosis. Two novel drugs are now approved to combat this disease: inotersen (Tegsedi®) [52] and patisiran (Onpattro®) [46]. Both of these drugs act to

reduce the amount of TTR protein (both wild type and mutant) produced in the liver, but by slightly different mechanisms. Inotersen is an antisense oligonucleotide inhibitor of TTR synthesis, whereas patisiran is a double-stranded small

interfering RNA (which targets a conserved sequence in the 3' UTR of mutant and wild-type TTR mRNA). Inotersen is administered subcutaneously, and patisiran is delivered by intravenous infusion in a lipid nanoparticle formulation.



# Tubulins

Other protein targets → Tubulins

**Overview:** Tubulins are a family of intracellular proteins most commonly associated with microtubules, part of the cytoskeleton. They are exploited for therapeutic gain in cancer chemotherapy as targets for agents derived from a variety of natural products: taxanes, colchicine and vinca alkaloids. These are thought to act primarily through  $\beta$ -tubulin, thereby interfering with the normal processes of tubulin polymer formation and disassembly.

## Further reading on Tubulins

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Nomenclature	tubulin alpha 1a	tubulin alpha 4a	tubulin beta class I	tubulin beta 3 class III	tubulin beta 4B class IVb	tubulin beta 8 class VIII
HGNC, UniProt	<a href="#">TUBA1A</a> , <a href="#">Q71U36</a>	<a href="#">TUBA4A</a> , <a href="#">P68366</a>	<a href="#">TUBB</a> , <a href="#">P07437</a>	<a href="#">TUBB3</a> , <a href="#">Q13509</a>	<a href="#">TUBB4B</a> , <a href="#">P68371</a>	<a href="#">TUBB8</a> , <a href="#">Q3ZCM7</a>
Inhibitors	–	–	vinblastine (pIC <sub>50</sub> 9), eribulin (pIC <sub>50</sub> 8.2) [78], paclitaxel (Mitotic cell cycle arrest in A431 cells) (pEC <sub>50</sub> 8.1) [83], colchicine (pIC <sub>50</sub> 8) [19], cabazitaxel, docetaxel, ixabepilone, vincristine	combretastatin A4 (pIC <sub>50</sub> 8.2) [28]	–	–

## SARS-CoV-2

Other protein targets → SARS-CoV-2

Coronaviruses are large, often spherical, enveloped, single-stranded positive-sense RNA viruses, ranging in size from 80–220 nm. Their genomes and protein structures are highly conserved. Three coronaviruses have emerged over the last 20 years as serious human pathogens: SARS-CoV was identified as the causative agent in an outbreak in 2002–2003, Middle East respiratory syndrome (MERS) CoV emerged in 2012 and the novel coronavirus SARS-CoV-2 emerged in 2019–2020. SARS-CoV-2 is the virus responsible for the infectious disease termed COVID-19 (WHO Technical Guidance 2020).

### Further reading on Tubulins

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## Structural proteins

Other protein targets → SARS-CoV-2 → Structural proteins

**Overview:** The virus particle has four structural proteins. The envelope, membrane and spike proteins are on the viral surface, while the polybasic nucleoprotein enables the tight coiling of the viral RNA.

Nomenclature	Envelope protein	Membrane glycoprotein	Nucleoprotein	Spike glycoprotein
Other names	envelope small membrane protein, orf4	Membrane protein	Nucleocapsid protein	Spike protein
UniProt	P0DTC4	P0DTC5	P0DTC9	P0DTC2
Function	By similarity to other coronavirus E proteins, SARS-CoV-2 E is predicted to constitute a single transmembrane (potentially homopentameric) ion channel with selectivity for monovalent cations over monovalent anions [85, 119, 133, 139]	The membrane glycoprotein (M) is usually regarded as the most abundant protein in the coronavirus envelope. By similarity with other coronavirus M proteins it is predicted to be essential for initiating assembly of the viral envelope components [94]	The coronavirus nucleocapsid phosphoprotein (N, or nucleoprotein) is highly basic and binds the viral RNA as a dimeric entity [25] into nucleocapsids which protect the viral genome, while also providing access for replication when required	The spike protein extends from the viral surface and binds to the host cell surface enzyme ACE2 to facilitate viral entry into the cell

## Polyproteins

Other protein targets → SARS-CoV-2 → Polyproteins

**Overview:** The viral RNA encodes two overlapping polyproteins which are cleaved autocatalytically by intrinsic proteases (see below).

Nomenclature	Replicase polyprotein 1a	Replicase polyprotein 1ab
Other names	Polyprotein 1a	Polyprotein 1ab
UniProt	P0DTC1	P0DTD1
Function	The replicase polyprotein 1a (pp1a) encodes a set of 11 smaller proteins, including two proteases that are responsible for cleaving the polyprotein chain into its component parts	The replicase polyprotein 1ab (pp1ab) encodes a set of 16 smaller proteins (5 more than pp1a)

**Comment:** The component proteins are non-structural and are involved in the transcription and replication of viral proteins and RNA.

## Proteases

Other protein targets → SARS-CoV-2 → Proteases

Nomenclature	3C-like (main) protease	Papain-like protease
Other names	3c-like proteinase, SARS-CoV-2 Mpro, Chain A, 3c-like Proteinase, 3CL protease, Mpro, nsp5	non-structural protein 3, NS3, nsp3, PL-PRO
UniProt	P0C6U8	P0DTC1
EC number	3.4.22.69	3.4.22.46
Function	The 3C-like protease cleaves the two polyproteins encoded by the SARS-CoV-2 genome (pp1a and pp1ab) into a range of non-structural proteins (nsp1-11 from pp1a; nsp1-16 from pp1ab). As these component proteins play crucial roles in viral replication, the 3C-like protease is considered to be a good molecular target for drug development. Small molecule 3C-like protease inhibitors would be predicted to reduce viral replication [33, 85]	The papain-like protease is a domain within coronavirus Nsp3. Its proteolytic activity cleaves three sites in the viral replicase polyprotein (recognition consensus sequence LXGG↓XX) to release the three non-structural proteins Nsp1, Nsp2, and Nsp3 [40]. It has additional non-proteolytic functions as part of the multicomponent replicase-transcriptase complex [103]

## Nucleic acid turnover

Other protein targets → SARS-CoV-2 → Nucleic acid turnover

Nomenclature	Non-structural protein 8	RNA-dependent RNA polymerase
Other names	Nsp8	non-structural protein 12, nsp12
UniProt	P0DTC8	P0DTD1
Function	Coronavirus nsp8 proteins form a hexadecameric complex with nsp7 proteins (8 subunits of each) [48, 122]. This complex may participate in viral replication by acting as a primase for de novo initiation of RNA synthesis	The conservation of RdRP catalytic domain between different RNA viruses endows inhibitors that were designed against other viral pathogens with activity against the SARS coronaviruses. Viral RdRP is the molecular target of nucleotide-based broad-spectrum antiviral compounds like remdesivir, tenofovir and ribavirin [33, 129, 141]

## Other proteins

Other protein targets → SARS-CoV-2 → Other proteins

Nomenclature	Protein 3a	Protein 7a	Protein 9b	Non-structural protein 6	Non-structural protein 7b
Other names	Orf3a	Orf7a	Orf9b, Accessory protein 9b, ORF-9b	Nsp6	Accessory protein 7b, nsp7b
UniProt	P0DTC3	P0DTC7	P0DTD2	P0DTC6	P0DTD8
Function	Protein 3a is a transmembrane pore-forming viral protein (viroporin) with potassium ion channel activity	The main function of the SARS-CoV protein 7a appears to be disruption of the host cell cycle and induction of caspase-dependent apoptosis [120]. By homology SARS-CoV-2 protein 7a is likely to produce the same effect	SARS-CoV protein 9b is a virion-associated accessory protein [120] that acts to block the host's ability to mount an antiviral IFN-induced innate immune response [87]. By homology, 9b from SARS-CoV-2 would be predicted to exhibit a similar function	Coronavirus nsp6 proteins limit autophagosome expansion [21]. This mechanism may favour coronavirus infection by damaging autophagosome-mediated delivery of viral components to lysosomes for degradation	Protein 7b is a coronavirus accessory protein. Experimental evidence suggests that SARS-CoV 7b has some attenuating function [87]. By homology, SARS-CoV-2 7b is likely to have a similar function

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